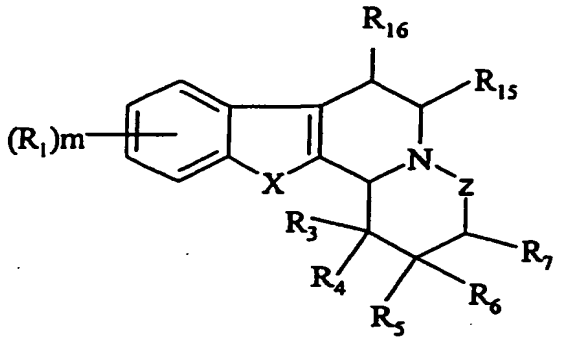
CLAIMS

1. Use of a compound of formula I,



I

wherein,

X is CR_2R_2', O, S or NR_2;

Z is $-CHR_8-(CH_2)n-$ or a single bond;

R_1 is hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halogen, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, CN, NO_2, NH_2, mono- or di(C_1-C_6)alkylamino or carboxyl;

R_2 and R_2' are independently H, hydroxy or (C_1-C_6)alkyl or R_2 and R_2' form, together with the carbon ring atoms to which they are attached, a carbonyl group;

R_3 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, NH_2, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino,mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or one of R_3 or R_4 and R_6 together form a bond between the ring atoms to which they are attached;

R_4 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_5 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) R_9 each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_7 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_8 is H,hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or, only when n is 0, R_7 and R_8 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) R_{10} each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-,

(C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

n is 0 or 1,

or a pharmaceutically acceptable salt or ester thereof, with the proviso, that the compound is not 1,2,3,4,5,10b-hexahydro-10-thia-3a-aza-cyclopenta[a]fluorine, for the manufacture of a medicament for the treatment of diseases or conditions where antagonists of alpha-2 adrenoceptors are indicated to be useful.

2. The use of a compound according to claim 1, wherein X is NR_2.

3. The use of a compound according to any one of claims 1 or 2, wherein m is 0, n is 0, R_2 is H, R_3 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO- or (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, R_4 is H, hydroxy, (C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl, R_5 is H, hydroxy, (C_1-C_6)alkyl or (C_1-C_6)alkoxy, R_6 is H or (C_1-C_6)alkyl and R_7 is H, (C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl.

4. The use of a compound according to any one of claims 1 to 3, wherein R_3 is H or (C_1-C_6)alkyl and R_4 is hydroxy or hydroxy(C_1-C_6)alkyl.

5. The use of a compound according to any one of claims 1 or 2, wherein R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed six membered saturated carbocyclic ring.

6. The use of a compound according to any one of claims 1 or 2, wherein R_4 and R_6 together form a bond between the ring atoms to which they are attached or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached.

7. The use of a compound according to any one of claims 1 to 5, wherein the compound is 1α-ethyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol, (1β-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-methanol, 1α-Methyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-ol, (1α-Methyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-yl)-methanol or 3,4,4aβ,5,6,7,8,13,13bβ,13cα-decahydro-2H-6a,13-diaza-indeno[1,2-*c*]phenanthren-1-one.

8. The use of a compound according to claim 1, wherein X is CR_2R_2'.

9. The use of a compound according to claim 1, wherein X is O

10. The use of a compound according to claim 1, wherein X is S.

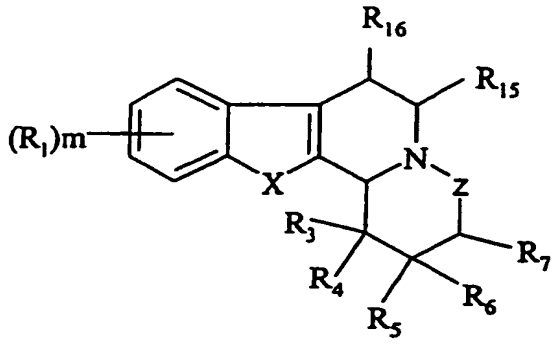
11. The use of a compound according to any one of claims 1 to 10, for the manufacture of a medicament for the treatment of a disorder of the central nervous system, diabetes, orthostatic hypotension, lipolytic disorders, Raynaud's disease or male and female sexual dysfunctions.

12. The use according to claim 11, wherein the disorder of the central nervous system is depression, anxiety disorders, post-traumatic stress disorder, schizophrenia, Parkinson's disease, or another movement disorder.

13. The use of a compound according to any one of claims 1 to 10 for the manufacture of a medicament for use as a selective alpha-2C antagonist.

14. The use according to claim 13 for the manufacture of a medicament for the treatment of mental disorders propagated by stress, Parkinson's disease, depression, negative symptoms of schizophrenia, attention deficit hyperactivity disorder, post-traumatic stress-disorder, or anxiety disorders.

15. A compound of formula IA



IA

wherein,

X is CR_2R_2', O or S;

Z is $-CHR_8-(CH_2)n-$ or a single bond;

R_1 is hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halogen, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, CN, NO_2, NH_2, mono- or di(C_1-C_6)alkylamino or carboxyl;

R_2 and R_2' are independently H, hydroxy or (C_1-C_6)alkyl or R_2 and R_2' form, together with the carbon ring atoms to which they are attached, a carbonyl group;

R_3 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, NH_2, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino,mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or one of R_3 or R_4 and R_6 together form a bond between the ring atoms to which they are attached;

R_4 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_5 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-

(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) R_9 each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_7 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_8 is H,hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or, only when n is 0, R_7 and R_8 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) R_{10} each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

n is 0 or 1,

or a pharmaceutically acceptable salt or ester thereof, with the provisos, that

a) when X is O, m is 0 and n is 0, then R_3-R_8 are not all simultaneously hydrogen;

b) the compound is not 1,2,3,4,5,10b-hexahydro-10-thia-3a-aza-cyclopenta[a]fluorene; 1,3,4,5,6,11b-hexahydro-2H-11-thia-4a-aza-benzo[a]fluorene; 1-(1,3,4,5,6,11b-hexahydro-2H-11-thia-4a-aza-benzo[a]fluoren-1-yl)-ethanone or 1,3,4,5,6,11b-hexahydro-2H-11-thia-4a-aza-benzo[a]fluorene-1-carboxylic acid methyl ester.

16. A compound according to claim 15, wherein X is CR_2R_2'.

17. A compound according to claim 15, wherein X is O.

18. A compound according to claim 15, wherein X is S.

19. A compound according to any one of claims 15 to 18, wherein R_3 is hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO- or (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl and R_4 is H, (C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl.

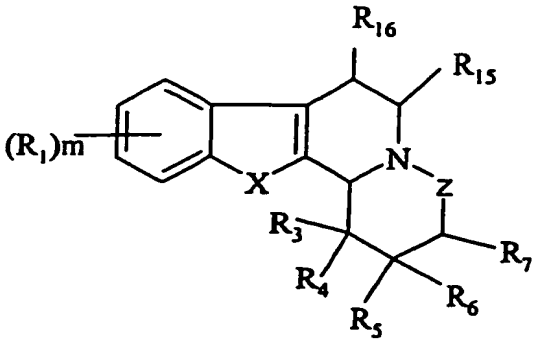
20. A compound according to any one of claims 15 to 19, wherein R_3 is hydroxy, hydroxy(C_1-C_6)alkyl or (C_1-C_6)alkoxy(C_1-C_6)alkyl and R_4 is (C_1-C_6)alkyl.

21. A compound according to any one of claims 15 to 18, wherein R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed six membered saturated carbocyclic ring.

22. A compound according to any one of claims 15 to 21, wherein the compound is 1α-Methyl-1,3,4,5,6,11b-hexahydro-2H-11-oxa-4a-aza-benzo[a]fluoren-1-ol, (1α-Methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-

methanol, (-)-(1α-Methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-methanol, (+)-(1α-Methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-methanol, 1α-Isopropyl-1,3,4,5,6,11b-Hexahydro-2H-11-oxa-4a-aza-benzo[a]fluoren-1-ol, 1α-Ethyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[a]fluoren-1-ol, (1α-Ethyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[a]fluoren-1-yl)-methanol, 1-Methyl-1α,3,4,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (1-Hydroxymethyl-1,3,4,5,6,11b-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl]-methanol, 1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (-)-1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (+)-1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, 1α-Methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene-1-carboxylic acid ethyl ester, 1-Ethoxymethyl-1α-methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (1α-Methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-methanol, (-)-(1α-Methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-methanol, (+)-(1α-Methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluoren-1-yl)-methanol, 1α–Ethyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa–4a-aza-benzo[*a*]fluorene-1-carboxylic methyl ester, 1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (-)-1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (+)-1-Methoxymethyl-1α-methyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene, (1α-Ethyl-1,3,4,5,6,11bα-hexahydro-2H-11-oxa-4a-aza-benzo[*a*]fluorene-1-yl)-methanol, acetic acid 1α-Methyl-1,3,4,5,6,11bβ-hexahydro-2H-11-oxa-4a-aza-benzo[a]fluoren-1-ylmethyl ester or (1α-Methyl-1,2,3,4,6,7,12,12bα-octahydroindeno[2,1-*a*]quinolizin-1-yl)-methanol.

23. A compound of formula IB



IB

wherein,

X is NR_2;

R_2 is $(C_1\text{-}C_6)$alkyl;

Z is $-CHR_8-(CH_2)n-$ or a single bond;

R_1 is hydroxy, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, halogen, halo$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-, CN, NO_2, NH_2, mono- or di$(C_1\text{-}C_6)$alkylamino or carboxyl;

R_3 is H, hydroxy, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_7)$cycloalkyl$(C_1\text{-}C_6)$alkyl, aryl, aryl$(C_1\text{-}C_6)$alkyl, aryloxy, aryl$(C_1\text{-}C_6)$alkoxy, aryloxy$(C_1\text{-}C_6)$alkyl, aryl$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, NH_2, amino$(C_1\text{-}C_6)$alkyl, mono- or di$(C_1\text{-}C_6)$alkylamino,mono- or di$(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-CO-, $(C_1\text{-}C_6)$alkyl-CO-O-, $(C_1\text{-}C_6)$alkyl-CO-O-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-, $(C_1\text{-}C_6)$alkoxy-CO-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy-CO-$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, carbamoyl, mono- or di$(C_1\text{-}C_6)$alkylcarbamoyl, carboxyl or $(C_1\text{-}C_6)$alkyl-S-$(C_1\text{-}C_6)$alkyl, wherein the said $(C_3\text{-}C_7)$cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, $(C_1\text{-}C_6)$alkyl, halogen, $(C_1\text{-}C_6)$alkoxy, NH_2, CN or NO_2, or one of R_3 or R_4 and R_6 together form a bond between the ring atoms to which they are attached;

R_4 is H, hydroxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy or $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl;

R_5 is H, hydroxy, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_7)$cycloalkyl$(C_1\text{-}C_6)$alkyl, aryl, aryl$(C_1\text{-}C_6)$alkyl, aryloxy, aryl$(C_1\text{-}C_6)$alkoxy, aryloxy$(C_1\text{-}C_6)$alkyl, aryl$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-CO-O-, $(C_1\text{-}C_6)$alkyl-CO-O-

(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) R_9 each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_7 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_8 is H,hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or, only when n is 0, R_7 and R_8 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) R_{10} each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

n is 0 or 1,

or a pharmaceutically acceptable salt and ester thereof, with the provisos, that

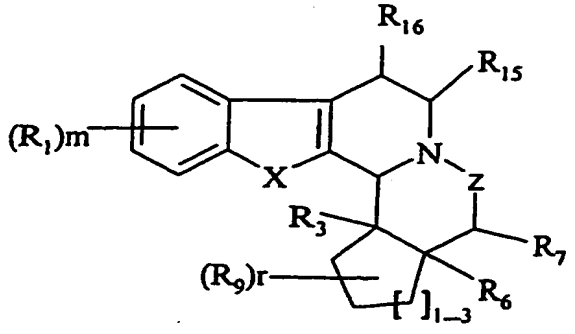
a) when m is 0 or R_1 is methoxy and R_4 is H or ethyl, then R_3 is not methoxy-CO;

b) the compound is not 12-Methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizine; 1-Ethyl-12-methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizine; 2,3-Diethyl-12-methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizine; 12-Methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizin-1-ol; 2-(1-Ethyl-12-methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-ethanol; 11-Methyl-2,3,5,6,11,11b-hexahydro-1H-indolizino[8,7-*b*]indole; (11-Methyl-2,3,5,6,11,11b-hexahydro-1H-indolizino[8,7-*b*]indol-1-yl)-methanol, (1,11-Diethyl-2,3,5,6,11,11b-hexahydro-1H-indolizino[8,7-*b*]indol-1-yl)-methanol or 3-(1-ethyl-12-methyl-1,2,3,4,6,7,12,12b-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-propionic acid methyl ester.

24. A compound according to claim 23, wherein R_3 is hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl or (C_1-C_6)alkoxy(C_1-C_6)alkyl and R_4 is H, (C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl.

25. A compound according to any one of claims 23 or 24, wherein the compound is 1α-Ethyl-12-methyl-1,2,3,4,6,7,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol or 1α-Ethyl-12-ethyl-1,2,3,4,6,7,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol.

26. A compound of formula IC



IC

wherein,

X is NR_2;

R_2 is H;

Z is $-CHR_8-(CH_2)n-$ or a single bond;

n is 0;

R_1 is hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halogen, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, CN, NO_2, NH_2, mono- or di(C_1-C_6)alkylamino or carboxyl;

R_3 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, NH_2, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_3 and R_6 together form a bond between the ring atoms to which they are attached;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_7 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_8 is H,hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or, only when n is 0, R_7 and R_8 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) R_{10} each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, $(C_1-$

C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_9 is hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

r is 1 to 3;

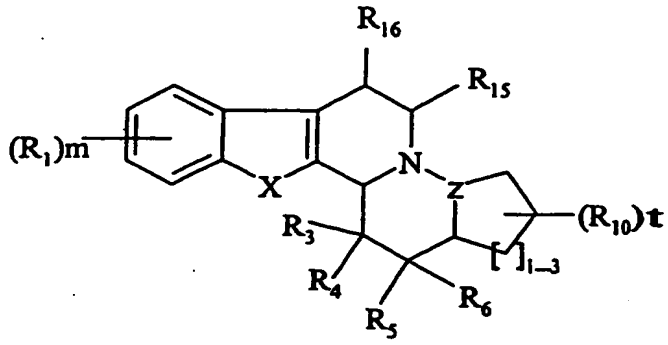
or a pharmaceutically acceptable salt and ester thereof, with the provisos, that the compound is not 10-methyl-5,7,7a,8,9,10,11,11a,11b,12-decahydro-6H-6a,12-diaza-indeno[1,2-*a*]fluorene; 3-hydroxy-1,2,3,4,4a,5,6,7,8,13,13b,13c-dodecahydro-6a,13-diaza-indeno[1,2-c]phenanthrene-4-carboxylic acid methyl ester; methyl-3-ethyl-1,2,3a,4,6,7,12b,12c-octahydro-3H,12H-indolo[2,3-*g*]cyclopent[a]indolizine-2-carboxylate; methyl-1,2,3a,4,6,7,12b,12c-octahydro-3H,12H-indolo[2,3-*g*]cyclopent[a]indolizine-2-carboxylate or 12c-ethyl-1,3a,4,6,7,12b,12c-octahydro-cyclopent[1,2]indolizino[8,7-b]indol-3(2H)-one.

27. A compound according to claim 26, wherein r is 1 and R_3 is H, hydroxy, (C_1-C_6)alkyl or hydroxy(C_1-C_6)alkyl.

28. A compound according to any one of claims 26 or 27, wherein the compound is 3,4,4aβ,5,6,7,8,13,13bβ,13cα-decahydro-2H-6a,13-diaza-indeno[1,2-*c*]phenanthren-1-one, 1,2,3,4,5,6,7,8,13,13b-decahydro-6a,13-diaza-indeno[1,2-

c]phenanthrene, acetic acid 1α,2,3,4,4aβ,5,6,7,8,13,13bβ,13cα-dodecahydro-6a,13-diaza-indeno[1,2-*c*]phenanthren-1-yl ester or acetic acid 1β,2,3,4,4aβ,5,6,7,8,13,13bβ,13cα-dodecahydro-6a,13-diaza-indeno[1,2-*c*]phenanthren-1-yl ester.

29. A compound of formula ID



ID

wherein,

X is NR_2;

R_2 is H;

Z is -CH-(CH_2)n-;

n is 0;

R_1 is hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halogen, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, CN, NO_2, NH_2, mono- or di(C_1-C_6)alkylamino or carboxyl;

R_3 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, NH_2, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or

NO_2, or one of R_3 or R_4 and R_6 together form a bond between the ring atoms to which they are attached;

R_4 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_5 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) R_9 each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_{10} is hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-

C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

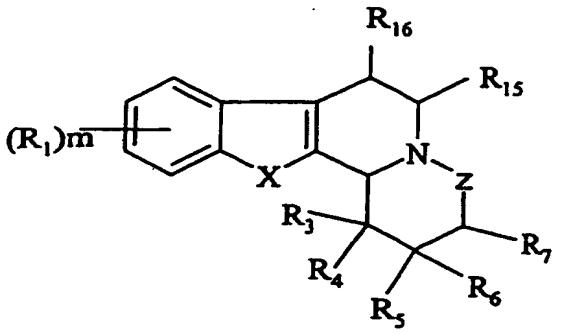
R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

t is 0 to 3;

or a pharmaceutically acceptable salt and ester thereof, with the provisos, that the compound is not 1,2,3,4,4a,5,6,11,11b,12,13,13a-dodecahydro-4b,11-diaza-indeno[2,1-*a*]phenanthrene; 1,2,3,4,4a,5,6,11,11b,12-decahydro-4b,11-diaza-indeno[2,1-*a*]phenanthrene; 9-methoxy-1,2,3,4,4a,5,6,11,11b,12-decahydro-4b,11-diaza-indeno[2,1-*a*]phenanthrene or 1-hydroxy-1,2,3,4,4a,5,6,11,11b,12,13,13a-dodecahydro-4b,11-diaza-indeno[2,1-*a*]phenanthrene-2-carboxylic acid methyl ester.

30. A compound of formula IE



IE

wherein,

X is NR_2;

R_2 is H;

Z is -CHR_8-(CH_2)n- or a single bond;

R_1 is hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halogen, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, CN, NO_2, NH_2, mono- or di(C_1-C_6)alkylamino or carboxyl;

R_3 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, NH_2, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino,mono- or di(C_1-

C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or one of R_3 or R_4 and R_6 together form a bond between the ring atoms to which they are attached;

R_4 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_5 is H, hydroxy, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_6)alkyl, aryl, aryl(C_1-C_6)alkyl, aryloxy, aryl(C_1-C_6)alkoxy, aryloxy(C_1-C_6)alkyl, aryl(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl, carboxyl or (C_1-C_6)alkyl-S-(C_1-C_6)alkyl, wherein the said (C_3-C_7)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, (C_1-C_6)alkyl, halogen, (C_1-C_6)alkoxy, NH_2, CN or NO_2, or R_4 and R_5 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) R_9 each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_6 is H, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or R_6 forms a bond between the ring atom to which it is attached and the ring atom to which R_7 is attached;

R_7 is H, hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R_8 is H,hydroxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy or (C_1-C_6)alkoxy(C_1-C_6)alkyl or, only when n is 0, R_7 and R_8 form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated

carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) R_{10} each independently being hydroxy, (C_1-C_6)alkyl, halogen, NH_2, NO_2, (C_3-C_7)cycloalkyl, hydroxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, carboxyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or oxo;

R_{15} is H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono- or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_1-C_6)alkyl-CO-, (C_1-C_6)alkyl-CO-O-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-(C_1-C_6)alkoxy(C_1-C_6)alkyl, carbamoyl, mono- or di(C_1-C_6)alkylcarbamoyl or carboxyl;

R_{16} is H or (C_1-C_6)alkyl;

R_7 and R_8 are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

n is 1,

or a pharmaceutically acceptable salt and ester thereof, with the proviso, that the compound is not 2,3,4,5,7,8,13,13b-octahydro-2,3-diethyl-1H-azepino[1',2':1,2]pyrido[3,4-*b*]indole; acetic acid 2,3,4,5,7,8,13,13b-octahydro-1H-azepino[1',2':1,2]pyrido[3,4-*b*]indol-2-ylmethyl ester; 2,3,4,5,7,8,13,13b-octahydro-1H-azepino[1',2':1,2]pyrido[3,4-*b*]indole-2-[(phenylmethoxy)methyl] or 2,3,4,5,7,8,13,13b-octahydro-1H-azepino[1',2':1,2]pyrido[3,4-*b*]indole-4-ethyl-2-[(phenylmethoxy)methyl].

31. A compound according to claim 30, wherein the compound is 2,3,4,5,7,8,13,13b-octahydro-1H-azepino[1',2':1,2]pyrido[3,4-*b*]indole.

32. A compound which is 2β-Methoxy-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizine, 2α-methoxy-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizine, 1α-Ethyl-2α-methyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol, 1α-Isopropyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol, (-)-1α-isopropyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-

a]quinolizin-1-ol, (+)-1α-isopropyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-ol, 1β-Isopropyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizine, (1α-Isopropyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-methanol, (1α- *n*-Propyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-methanol, 2-(1α,2,3,4,6,7,12,12bβ-Octahydro-indolo[2,3-*a*]quinolizin-1-yl)-butan-2-ol, 1-(1,2α,3,4,6,7,12,12bα-Octahydro-indolo[2,3-*a*]quinolizin-2-yl)-propan-1-ol, 2-(1α,2,3,4,6,7,12,12bβ-Octahydro-indolo[2,3-*a*]quinolizin-1-yl)-propan-2-ol, 1-*s*-Butyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-ol, 1-Cyclohexyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-ol, 9-Fluoro-1α-isopropyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-ol, (1α-Methyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-yl)-methanol, (-)-(1α-Methyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-yl)-methanol, (+)-(1α-Methyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-1-yl)-methanol, (1α-Ethyl-1,4,6,7,12,12bβ-hexahydroindolo[2,3-*a*]quinolizin-1-yl)-methanol, 3β,4α-Dimethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizine, (1,2α,3,4,6,7,12,12bα-Octahydroindolo[2,3-*a*]quinolizin-2-yl)-propan-2-ol, (1,2α,3,4,6,7,12,12bβ-Octahydroindolo[2,3-*a*]quinolizin-2-yl)-propan-2-ol, (2α-Ethyl-1,2,3,4,6,7,12,12bα-octahydroindolo[2,3-*a*]quinolizin-2-yl)-methanol, (2α-Ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-*a*]quinolizin-2-yl)-methanol, (1-αEthyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-a]quinolizin-1-ylmethoxy)-acetic acid ethyl ester, 1-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-2-yl)-ethanone, 1-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-2-yl)-ethanol, 2-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-2-yl)-propan-2-ol, 2-(3-ethyl-1,2α,3α,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-2-yl)-propan-2-ol, (3-ethyl-2-methyl-1α,2β,3β,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1-yl)-methanol, 3-ethyl-1,2-dimethyl-1α,2β,3β,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizine, 1,2-dimethyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizin-1β-ol, (1-ethyl-2-methyl-1β,2β,3β,4,6,7,12,12bα-octahydro-indolo[2,3-*a*]quinolizin-3-yl)-methanol, 1-β-Hydroxymethyl-1-methyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-*a*]quinolizine-6β-carboxylic acid methyl ester,

5,6,7,7aβ,8,9,10,11,11aβ,11bα-Decahydro-12-oxa-6a-aza-indeno[1,2-*a*]fluorene, 2,3,4,4aβ,5,6,7,8,13bβ,13cβ-Decahydro-1H-13-oxa-6a-aza-indeno[1,2-*c*]phenanthrene, 2,3,4,4aβ,5,6,7,8,13bα,13cβ-Decahydro-1H-13-oxa-6a-aza-indeno[1,2-*c*]phenanthrene, 2,3,4,4aβ,5,6,7,8,13,13bβ-decahydro-1H-6a,13-diaza-indeno[1,2-*c*]phenanthren-13cβ-ol, (-)-2,3,4,4aβ,5,6,7,8,13,13bβ-decahydro-1H-6a,13-diaza-indeno[1,2-*c*]phenanthren-13cβ-ol, (+)-2,3,4,4aβ,5,6,7,8,13,13bβ-decahydro-1H-6a,13-diaza-indeno[1,2-*c*]phenanthren-13cβ-ol, (2,3,4,4aβ,5,6,7,8,13,13bβ-Decahydro-1H-6a,13-diaza-indeno[1,2-*c*]phenanthrenyl)-13cβ-methanol or 5,6,7,7a,11,11b,12-Decahydro-6a,12-diaza-indeno[1,2-*a*]fluoren-11a-ol.

33. A pharmaceutical composition comprising at least one compound according to any one of claims 15 to 32 and a pharmaceutically acceptable diluent, carrier and/or excipient.

34. A compound according to any one of claims 15 to 32 for use as a medicament.

35. A method for the treatment of a disease or condition where an antagonist of alpha-2 adrenoceptors is indicated to be useful, which comprises administering to a mammal in need of the treatment an effective amount of at least one compound according to claim 1.

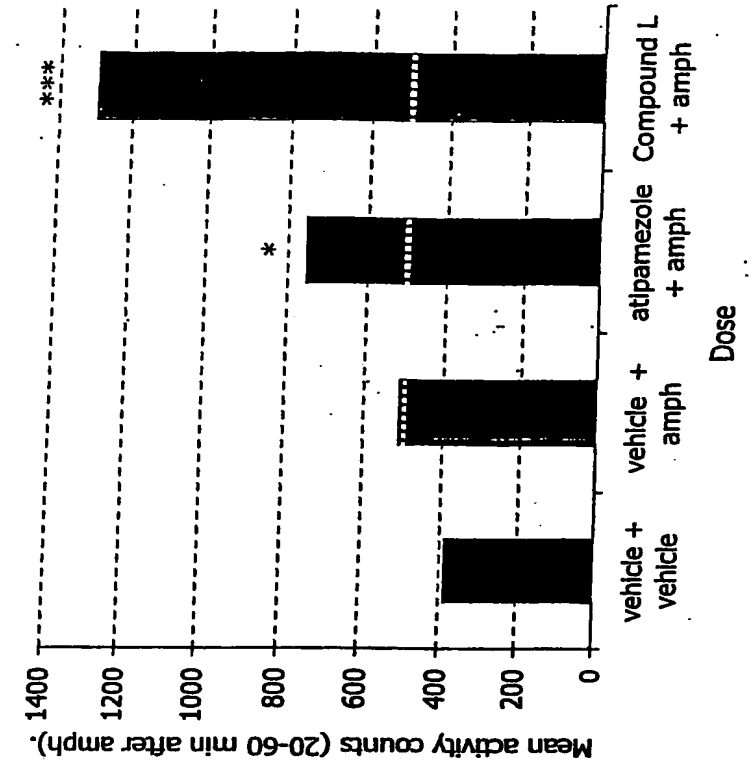

Mean activity counts (20-60 min after amph).
1400
1200
1000
800
600
400
200
0
***
*
vehicle + vehicle
vehicle + amph
atipamezole + amph
Compound L + amph
Dose

FIG. 1b

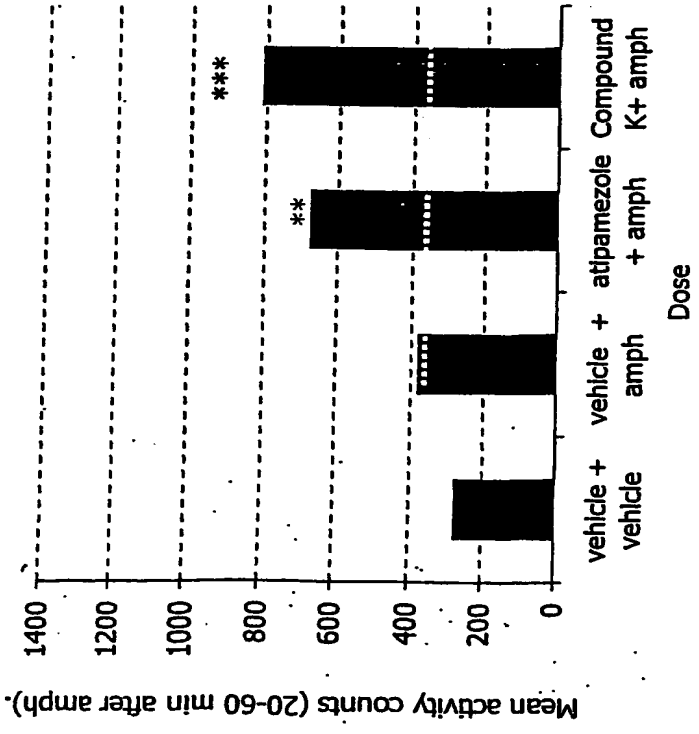

Mean activity counts (20-60 min after amph).
1400
1200
1000
800
600
400
200
0
***
**
vehicle + vehicle
vehicle + amph
atipamezole + amph
Compound K+ amph
Dose

FIG. 1a

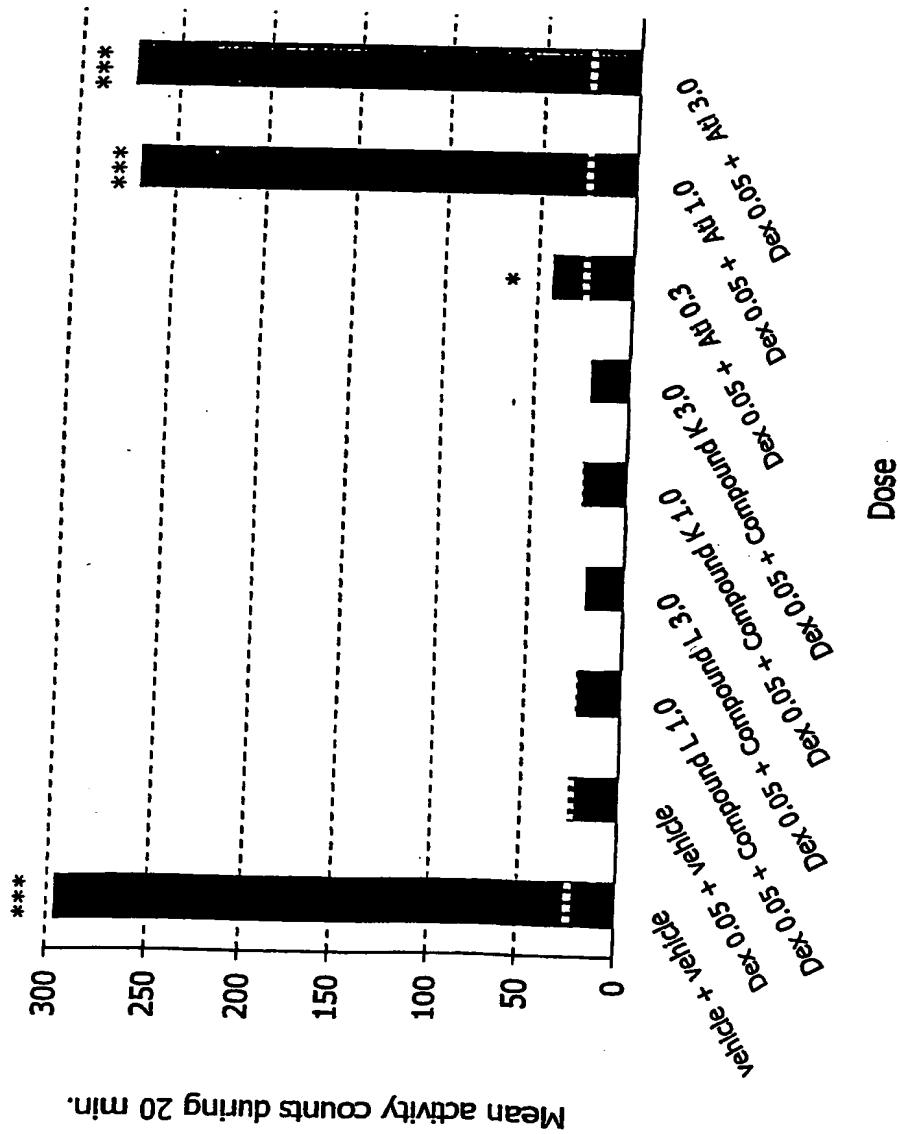

Mean activity counts during 20 min.
300
250
200
150
100
50
0
***
***
***
*
Vehicle + Vehicle
Dex 0,05 + Vehicle
Dex 0,05 + Compound L 1,0
Dex 0,05 + Compound L 3,0
Dex 0,05 + Compound K 1,0
Dex 0,05 + Compound K 3,0
Dex 0,05 + Ad 0,3
Dex 0,05 + Ad 1,0
Dex 0,05 + Ad 3,0
Dose

FIG. 2

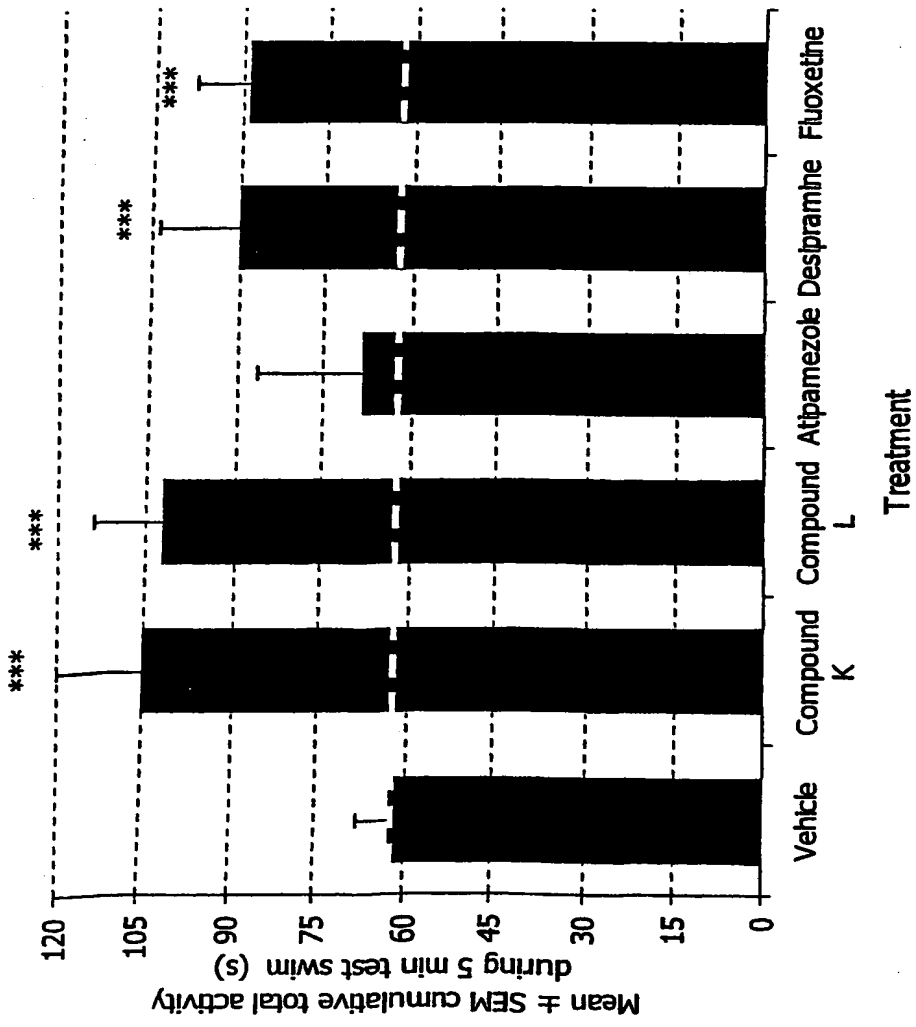

Mean ± SEM cumulative total activity
during 5 min test swim (s)
120
105
90
75
60
45
30
15
0
***
***
***
***
Vehicle
Compound K
Compound L
Atipamezole
Desipramine
Fluoxetine
Treatment

FIG 3.

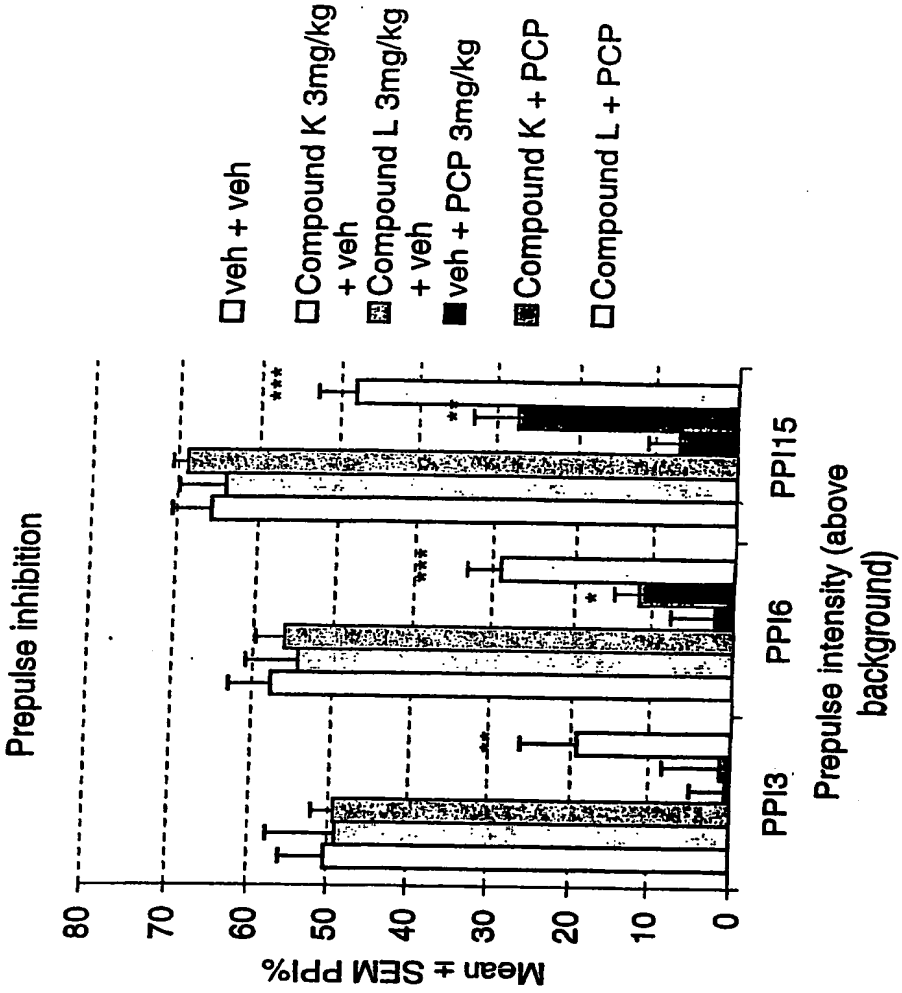

veh + veh
Compound K 3mg/kg + veh
Compound L 3mg/kg + veh
veh + PCP 3mg/kg
Compound K + PCP
Compound L + PCP
Prepulse inhibition
Mean ± SEM ppi%
Prepulse intensity (above background)
PPI3
PPI6
PPI15

FIG. 4b

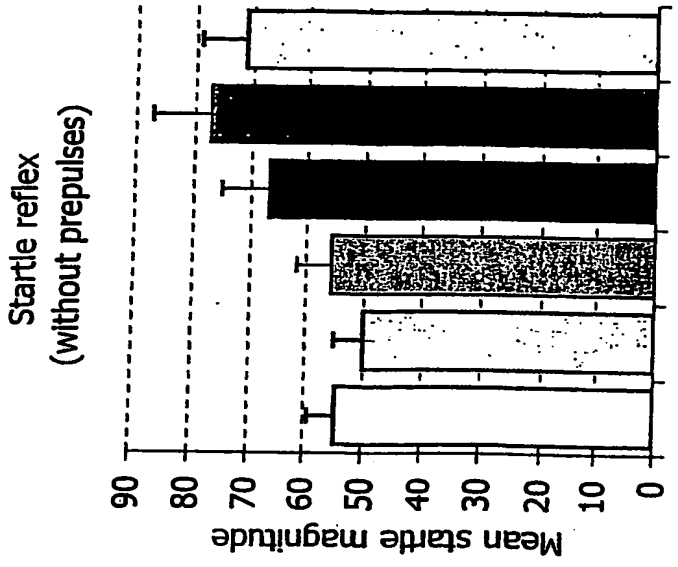

Startle reflex (without prepulses)
Mean startle magnitude

FIG. 4a

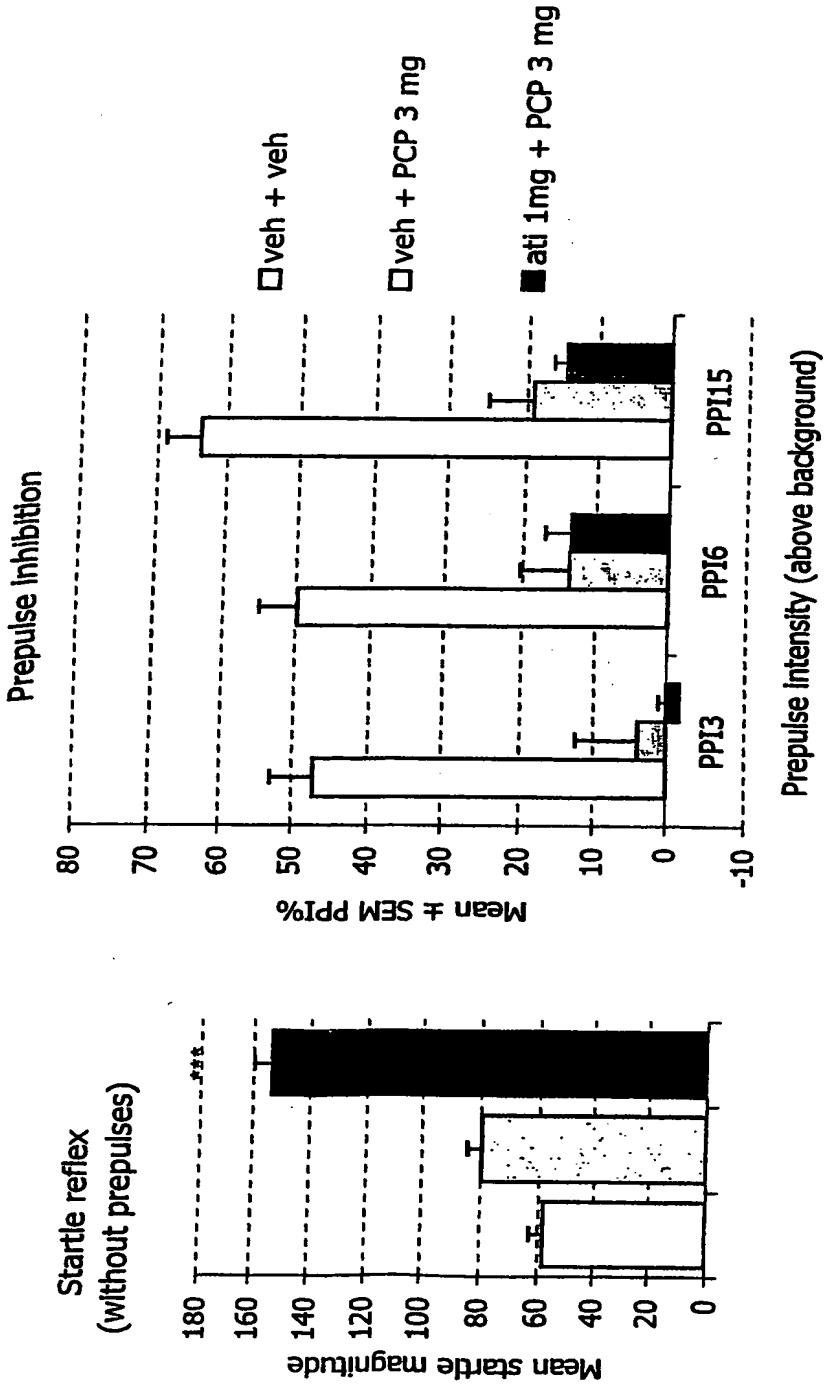

Prepulse Inhibition
veh + veh
veh + PCP 3 mg
ati 1mg + PCP 3 mg
Mean ± SEM ppi%
80
70
60
50
40
30
20
10
0
-10
PPI3
PPI6
PPI15
Prepulse intensity (above background)

FIG.5b

Startle reflex
(without prepulses)
***
Mean startle magnitude
180
160
140
120
100
80
60
40
20
0

FIG. 5a

INTERNATIONAL SEARCH REPORT

International Application No
PCT/FI 03/00255

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D455/00 C07D471/04 C07D491/147 C07D495/14 A61K31/55
A61K31/4375 A61P3/06 A61P3/10 A61P9/02 A61P15/10
A61P25/00 A61P25/14 A61P25/16 A61P25/18 A61P25/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 686 226 A (HUFF JOEL R ET AL) 11 August 1987 (1987-08-11) column 1, line 7 - line 58 column 2, line 27 - line 35; examples Alfa2-adrenergic antagonists with use as antidepressives and antidiabetics and satisfying claims 1,9 and 10-14 ---	1-35
X	EP 0 213 793 A (WYETH JOHN & BROTHER LTD) 11 March 1987 (1987-03-11) abstract; examples column 9, line 23 - line 30; claims Analogous alfa2-adrenergic antagonists with use as, e.g., antidepressives and antidiabetics --- -/--	1-35

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2003	21 07 2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	PER RENSTRÖM /EÖ

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE STN INTERNATIONAL [Online] File CAPLUS, CAPLUS accession no. 1999:246819, Document no. 131:53570; GRIFFITH, RENATE ET AL: "Modeling of adrenoceptor ligand targets based on novel medium- or macro-sized fused nitrogen heterocyclic systems" XP002245426 & Journal of Computer-Aided Molecular Design (1999), 13(1), 69-78, Compound satisfying formula I with alpha2-adrenergic activity; proviso compound in claim 15 abstract	1,3-6, 9-15, 17-22, 33-35
X	DATABASE STN INTERNATIONAL [Online] File CAPLUS, CAPLUS accession no. 1981:533210, Document no. 95:133210 ; BOELSING, EKKEHARD ET AL: "Reactions of indole derivatives. XLVI. Stereoselective route to isoeburnamonine" XP002245427 & Chemische Berichte (1981), 114(5), 1932-7, Compounds satisfying formula IC abstract	26,27,30
X	DATABASE STN INTERNATIONAL [Online] File CAPLUS, CAPLUS accession no. 1978:597770, Document no. 89:197770; POGOSYAN, S. A. ET AL : "Indole derivatives. LX. 1,2,3,4,4a,5,7,8,13b,13c-Decahydro-13H-benz(g)indolo(2,3-a)indolizines and 1,2,3,4,4a,5,7,8,9,14,14b,14c-dodecahydroisoindolo(1,2-a)indolo(2,3-c)azepines" XP002245428 & Armyanskii Khimicheskii Zhurnal (1978), 31(4), 260-6, Compound satisfying formula IC with analgesic properties abstract	1-6,11, 23,24, 26,27, 30,33-35
X	DATABASE STN INTERNATIONAL [Online] File HCAPLUS, HCAPLUS accession no. 2001:855109, Document no. 137:88229; ABDEL-ZAHER, AHMED O. ET AL: "The potential antidiabetic activity of some alpha-2 adrenoceptor antagonists " XP002245429 & Pharmacological Research (2001), 44(5), 397-409 abstract	1-6, 11-14, 23,24, 33-35

-/--

INTERNATIONAL SEARCH REPORT

International Application No
PCT/FI 03/00255

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RIKU AANTAA MD: "Alpha2-adrenoceptor antagonists" BAILLIÈRE'S CLINICAL ANAESTHESIOLOGY, vol. 14, no. 2, 2000, pages 285-292, XP002245599 the whole document ---	1-6, 11-14, 23,24, 33-35
X	GUAY AT ET AL: "Yohimbine treatment of organic erectile dysfunction in a dose-escalation trial." INT J IMPOT RES., vol. 14, no. 1, February 2002 (2002-02), pages 25-31, XP002245425 the whole document -----	1-6, 11-14, 23,24, 33-35

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 35

Claim 35 relates to a method of treatment of the human or animal body by surgery or by therapy/a diagnostic method practised on the human or animal body Rule 39.1(iv). Nevertheless, a search has been executed for this claim. The search has been based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 1-35

The expressions "diseases or conditions where antagonists of alpha-2-adrenoreceptors are indicated to be useful" in claims 1-10, "disorder of the central nervous system" and "lipolytic disorders" in claim 11,"movement disorder" in claim 12, "for use as a selective alpha-2C antagonist" in claim 13 and "mental disorders propagated by stress" in claim 14 may relate to a large number of different disorders and conditions which cannot be clearly defined by these expressions. The claims are in violation with the requirements of Article 6 PCT that claims shall be clear and concise. The search has therefore been limited to the other, more clearly defined, diseases and groups of diseases mentioned in the present claims 11-12 and 14.

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible.
Consequently, the search has been restricted to:

claims 1-15 related to the compounds of claims 15-32,
claims 16, 18-20, 22, 24-29 and 31-32,
claim 30 for Z = -CHR8-(CH2)n- and
claims 33-34 related to the compounds of claims 16, 18-20, 22, 24-29, 31-32 and claim 30 for Z = -CHR8-(CH2)n-.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INT[redacted]ATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/FI 03/00255

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4686226 A	11-08-1987	DE 3675714 D1	03-01-1991
		EP 0214556 A1	18-03-1987
		JP 62111986 A	22-05-1987
EP 0213793 A	11-03-1987	AT 73804 T	15-04-1992
		AU 582663 B2	06-04-1989
		AU 6080486 A	12-02-1987
		CA 1308720 C	13-10-1992
		DE 3684384 D1	23-04-1992
		DK 380286 A ,B,	11-02-1987
		EP 0213793 A2	11-03-1987
		ES 2003086 A6	16-10-1988
		GB 2178741 A ,B	18-02-1987
		GR 862077 A1	24-12-1986
		HU 45054 A2	30-05-1988
		IE 59304 B1	09-02-1994
		JP 1955829 C	28-07-1995
		JP 6084374 B	26-10-1994
		JP 62039586 A	20-02-1987
		KR 9406630 B1	23-07-1994
		PT 83154 A ,B	01-09-1986
		US 4788202 A	29-11-1988
		ZA 8605844 A	30-03-1988
US 3492303 A	27-01-1970	NONE	
EP 0130823 A	09-01-1985	HU 34974 A2	28-05-1985
		CA 1248958 A1	17-01-1989
		DK 317284 A	30-12-1984
		EP 0130823 A2	09-01-1985
		FI 842236 A	30-12-1984
		JP 60045581 A	12-03-1985
		US 4587251 A	06-05-1986

INTERNATIONAL SEARCH REPORT

International Application No
PCT/FI 03/00255

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P25/24 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 492 303 A (MORRISON GLENN CURTIS ET AL) 27 January 1970 (1970-01-27) column 1, line 24 -column 2, line 20 column 5 -column 9; examples 3-12 Compounds satisfying claims 1-3, 5 and 11-14, for use as central nervous system depressants ---	1-7, 11-14, 23-35
X	EP 0 130 823 A (RICHTER GEDEON VEGYESZET) 9 January 1985 (1985-01-09) Compounds satisfying formuls IC in claim 26, whith pharmacological properties --- -/--	26,27, 30,33,34

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2003	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	PER RENSTRÖM /EÖ

INTERNATIONAL SEARCH REPORT

ational application No.
PCT/FI 03/00255

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 35
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 1-35
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.